REMARKS

Claim 16 has been cancelled by the present amendment without prejudice to pursing it in a subsequent application. Claims 13-15 remain pending in the application. As requested by the Examiner, Applicants are sending with this paper a new copy of the declaration and copies of references 1-4 cited in the December 21, 2001 Information Disclosure Statement. Applicants respectfully request that the Examiner consider these references. Applicants acknowledge and appreciate that the Examiner has withdrawn rejections under 35 U.S.C. § 101 and 35 U.S.C. § 112, ¶ 2. Applicants have carefully considered all of the remaining and pending rejections but respectfully assert that the pending claims are allowable over the Examiner's rejections for at least the reasons set forth below.

Rejections under § 112

The Examiner has rejected Claims 13-16 under 35 U.S.C. § 112, ¶ 1 for failing to comply with the enablement requirement. Applicants acknowledge and appreciate that the Examiner has found that "the specification does enable the generation of an interaction fingerprint." Office Action, page 6. However, the Examiner asserted that nothing in the specification enables the identification of a target protein for pharmaceutical intervention because there are no parameters set forth as to the meaning of the fingerprints in terms of disease. The Examiner asserted that it is unclear how one would get to step (f) from steps (a)-(e) of Claim 13. Specifically, the Examiner posed several questions including: 1) How does the protein fingerprint tell anything pertinent to a target for pharmaceutical intervention? 2) What do the binding affinity values mean in terms of pharmaceutical intervention? 3) Is binding a positive indicator or a negative indicator? 4) Are degrees of binding assessed? 5) What is the correlation between the fingerprint and a disease? and 6) What do repeated comparisons have to do with identification of a potential protein target. *See* Office Action, pages 4 and 6.

After discussing the generation of interaction fingerprints, which the Examiner acknowledged is enabled, the specification describes one way in which interaction fingerprints can be compared. *See* Specification, page 8, lines 5-23 and figure 5. Specifically, the specification describes an "overlap computation," which comprises a vector multiplication of the two interaction fingerprints. The overlap value can optionally be normalized. The Specification

indicates that normalized overlap values closer to one indicate proteins with similar chemical response while values closer to zero indicate proteins with divergent chemical response. *See* Specification, page 8, lines 27-28. This correlation between interaction fingerprint overlap and the comparative chemical responses naturally follows because proteins with similar interaction fingerprints (e.g., proteins that bind to a similar set of chemical ligands) can be expected to have similar chemical response. Therefore, the Specification enables one of skill in the art to generate interaction fingerprints for a plurality of proteins, compare those interaction fingerprints to determine the degree of overlap, and use the degree of overlap as an indication of the proteins' chemical similarity or dissimilarity.

The Specification provides several non-limiting examples of how the determination of chemical similarity or dissimilarity of proteins can be used to identify a potential target protein for pharmaceutical intervention. In one example, a protein can be identified for pharmaceutical intervention out of several proteins that are targets of a drug candidate. The interaction fingerprint of each potential target protein is compared with the interaction fingerprints of other proteins in the human genome. *See* Specification, page 9, lines 4-10. If the there is high overlap between the interaction fingerprints of the potential target protein and any of the other human genome proteins, then there is a likelihood that the potential target protein is not a good candidate for pharmaceutical intervention because undesirable side effects can be expected (i.e., targeting the protein for intervention will also interfere with other biochemical pathways in the body). Thus, the potential target protein that has the least overlap with other human genome proteins can be selected as a target protein for pharmaceutical intervention because it will have the least side effects. In this example, a low overlap of interaction fingerprints indicates that a potential target protein is suitable for pharmaceutical intervention.

In a related example, the interaction fingerprints of multiple proteins known to be involved in a metabolic pathway of a disease pathogen are compared with the interaction fingerprints of proteins in the human genome. *See* Specification, page 10, lines 4-17. The protein out of the multiple metabolic proteins that has the lowest average and/or maximum overlaps with the human proteins may be identified as a protein for pharmaceutical intervention because targeting that protein is expected to result in low side effects. Thus, in this example, a

low overlap of interaction fingerprints between the identified pathogen metabolic protein and human proteins indicates that the target protein is suitable for pharmaceutical intervention.

Another example in the specification describes comparing the interaction fingerprints of a family of related proteins. *See* Specification, page 10, line 26 to page 11, line 6. Although the interaction fingerprints of related proteins are likely to be similar, there may be regions of the fingerprint that are different. Thus, a protein within the family can be identified as suitable for pharmaceutical intervention if there is a region of the interaction fingerprint that differs from other proteins in the family. Such a region indicates chemical ligands that might preferentially bind to the protein but not to other proteins in the family.

In still another example, high overlap of interaction fingerprints of proteins can indicate that the proteins are members of the same functional family, subfamily, or family tree. *See* Specification, page 11, lines 8-13. Thus, one of skill in the art would recognize that a protein could be identified as a target for pharmaceutical intervention if its interaction fingerprint had high overlap with other proteins that had already been determined to be effective targets for pharmaceutical intervention.

Thus, as demonstrated by the extensive discussion and practical examples as described above, the Specification provides enabling disclosure that teaches those of skill in the art how to use the claimed invention. Specifically, the Specification teaches several ways to compare interaction fingerprints and then use that comparison to identify proteins as target proteins for pharmaceutical intervention. The Applicants have addressed the Examiner's concerns regarding getting from steps (a)-(e) of Claim 13 to step (f) by demonstrating that the Specification teaches several ways of how to use the comparison of interaction fingerprints (i.e., steps (d) and (e)) to identify a potential target protein as a target protein for pharmaceutical intervention (i.e., step (f)). With regard to Examiner's questions 1 through 5 as identified above, the Applicants point out that while the specification does discuss ways that interaction fingerprints can be used alone (*see e.g.*, Specification, page 10, lines 19-24), Claims 13-15 require the step of comparing interaction fingerprints and Claim 16 requires a search and computation engine configured to compare interaction fingerprints. Thus, enablement of Claims 13-16 does not require teaching how to use interaction fingerprints and the binding affinities they represent in isolation in order to identify targets for pharmaceutical intervention. Rather, it has been demonstrated above how the

specification teaches to use the ***comparison*** of interaction fingerprints to make such identifications. Thus, the Applicants have answered the Examiner's question 6 by showing that the Specification teaches how a comparison of interaction fingerprints can lead to identification of a potential target protein for pharmaceutical intervention. Accordingly, the Applicants respectfully submit that Claims 13-16 are fully enabled by the Specification and that they have addressed all of the Examiner's concerns with respect to enablement.

Rejections under § 102

The Examiner has rejected Claim 16 under 35 U.S.C. § 102(a) as being anticipated by Xenarios et al. (Nucleic Acids Research (2000) Vol. 28, pages 289-291). The Examiner asserts that Xenarios et al. teaches a database of interacting proteins that includes sequence information and protein interactions and that the database can be searched. The Applicants respectfully submit that Xenarios et al. does not disclose interaction fingerprints or the comparison of interaction fingerprints. Claim 16 required a search ***and computation*** engine configured to retrieve ***and compare*** interaction fingerprints. The Examiner has not argued that Xenarios et al. discloses computation or comparison functionality. Nonetheless, in order to advance prosecution, the Applicants have cancelled Claim 16 without prejudice to pursuing it in a continuation application. Therefore, it is respectfully submitted that the rejection under § 102 is moot.

CONCLUSION

The Applicants respectfully submit that they have addressed all the Examiner's concerns regarding Claims 13-15 by the remarks above. As such, the Applicants request that Claims 13-15 be allowed.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 8/12/04

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